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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,846	01/25/2002	Calvin Roskelley	SMAR-020	1574

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EXAMINER	
HABTE, KAHSAY	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,846	ROSKELLEY ET AL.	
	Examiner	Art Unit	
	Kahsay Habte, Ph. D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17,18,20,40-44,46 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17,40-44,46 and 51-54* is/are rejected.

7)☒ Claim(s) *18 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-15, 17-18, 20, 40–44, 46 and 51-54 are pending.

Response to Amendment

2. Applicant's amendment filed 9/02/2004 in response to the previous Office Action (3/3/2004) is acknowledged. Rejections of claims 1-15, 17-18, 20 and 40-44, 46 and 51-54 under 35 U.S.C. § 112, second paragraph (paragraphs 6a-6b and 6d) have been obviated. The enablement rejection (item 5) and the second paragraph rejection (items 6c and 6e) have been maintained.

Objection

3. Claims 18 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-44 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There has been recited a method of inhibiting cellular invasions or angiogenesis in a patient, but the specification is not enabled for such a scope.

According to the specification (pages 1-2), inhibition of cellular invasions or angiogenesis is useful for the treatment of cancer. Thus, the claim is drawn to a method of treating cancer in general. The claim sets forth the treatment of cancer generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Response to arguments

Applicants' arguments filed 09/02/2004 has been fully considered but it is not persuasive.

Applicants disagree with the Examiner in regard to lack of enablement. To support their argument, applicants cite a case law (Amgen v. Chugai (1991)18 USPQ 2d 1016 at 1027) and also point out to (MPEP 2164.01 p2100-179) that reads "sufficient information regarding the subject matter of the claims as to enable one skilled pertinent art to make and use the claimed invention". The examiner disagrees with applicants. There is no sufficient information regarding the subject matter of the claims as to enable one skilled pertinent art to make and use the claimed invention. The disclosure is not sufficient to enable one skilled in the art to carry out the invention. This is the reason why the examiner made the rejection at first place. Inhibition of cellular invasion or angiogenesis as disclosed in the specification (pages 1-2) is useful for the treatment of cancer generally. Thus, inhibition of cellular invasion or angiogenesis amounts to the same thing as a method of treating cancer generally. Applicants did not answer any

questions regarding the treatment of cancer. This indicates that one skilled in the art could not carry the invention i.e. inhibit cellular invasion or angiogenesis for the treatment of cancer generally.

Applicants also argue: "The specification clearly teaches inhibition of cellular invasion and angiogenesis by numerous compounds falling within the scope of the claims in a variety of different assays and in a variety of cell types, both *in vitro* and *in vivo* (p. 23-28)." The examiner disagrees with applicants. In pages 23-28, there are some IC_{50} data on the inhibition of cellular invasion ranging from 1-10 micro molar, but the tests presented in the drawing (FIG. 1-12) are not straightforward. One skilled in the art would not able to interpret the graphs presented in said figures. The "% Invasion inhibition" on the y-axis is unclear to what it is referring. What is measured in the y-axis of the graphs in FIG. 1-14? What is inhibited? What types of cancer cells were used in the test? In general, the graphs presented in FIG. 1-14 are ambiguous. One skilled in the art would not able to interpret the data as presented in said figures. From the data presented in FIG. 1-14, there is no way to link the concentration data in the x-axis to the method of inhibition or to the method of treating cancer generally. Applicants have presented data on page 27 of the specification, but the tests were done only for 2 tumor models, one a lung tumor and the other, SCCVII. Note that the test for lung tumors and SCCVII tumors could not be used as a representative test for cancer generally let alone all cellular invasions. Since applicants disclose that inhibition of cellular invasions or angiogenesis is useful for the treatment of cancer, it is up to applicants to show that the

treatment of cancer generally can be achieved by inhibiting cellular invasion or angiogenesis.

Since cellular invasion is very broad and it can include two definitions:

a. Cells being invaded by something else e.g. viruses, prions, etc., or

b. Cells are invading parts of the body (fungi, bacteria); the claim covers more than just cancers. It covers the treatment of pathogenic diseases in general. Note that there is no such agent to treat pathogenic diseases in general, because pathogenic diseases are extremely broad. Some pathogenic diseases are caused by bacteria (i.e. meningitis, whooping cough, tetanus, syphilis, etc.), some are caused by virus (i.e. HIV, common cold, measles, chicken pox, etc), some are caused by fungus (i.e. athletic foot, etc.), some are caused by protozoa (i.e. Amebiasis, Giardiasis, Lesihmaniasis, Beaver fever, Toxoplasmosis, Trichomoniasis, etc.). Not only that the viral diseases are different from bacterial and fungal diseases, but the viral diseases as listed above are also different one from the other. The nature of effect, origin, symptom, incubation, diagnosis, etc., is different one from the other. The same is true for the bacteria caused diseases and fungal caused diseases.

For example, HIV (human immunodeficiency virus) is a human T-cell leukemia/lymphoma virus of the subfamily Lentivirinae that is the causative agent of the disease AIDS. AIDS is an acquired immunodeficiency syndrome, an epidemic retroviral disease due to infection with human immunodeficiency virus (HIV-1), transmissible via blood or semen, and characterized by an ineffective immune response; the disease follows a protracted and debilitating course and has a poor prognosis.

Applicants can provide a recent scientific publication that shows the treatment of pathogenic diseases generally or the treatment of cancer in general by inhibiting cellular invasion or angiogenesis.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15, 17, 40-44, 46 and 51-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a. In claim 1 (page 2) or elsewhere in the claims, the variables "NR^3+" lacks a counter anion. What are the counter anions? Applicants have to recite the counter anions in the claim, assuming there is descriptive support for it. The same problem exists with the quaternary amine in formula II.

Response to arguments

Applicants' arguments filed 09/02/2004 has been fully considered but it is not persuasive.

Applicants argue: "It is well known in the art that compounds may exist in a charged form, and the identity of the counter ion of a given charged moiety of a compound in a given environment is not necessary to know the metes and bounds of

the claimed compound." The examiner disagrees with applicants. A compound must be neutral. Even if a compound exists as charged, a counter ion must be present. The claim does not provide for any counter ion when X is substituted by $-NR_3+$.

b. Claim 40 is rejected because the phrase "cellular invasion" is indefinite. Are the cells being invaded by fungi, bacteria, virus, etc. or the cells are invading other parts of the body? This is not a standard medical terminology.

Response to arguments

Applicants' arguments filed 09/02/2004 has been fully considered but it is not persuasive.

Applicants argue by indicating to page 1 (lines 20-28) of the specification that discloses the meaning of the phrase. Applicants argue: "cellular invasion is invasion by a cell of other parts of a body, and not invasion of an agent into a cell". The examiner disagrees with applicants. The specification (page 1, lines 20-28) as shown below:

> Inhibition of cell motility and invasion would be useful for the treatment of cancer, and other disorders involving cell motility and invasion including those listed above, as well as for contraception. For example, cancer cell invasion driven by altered interactions between cells and an extracellular matrix (ECM). In the case of epithelial-derived carcinomas, the primary tumour is surrounded by a specialized ECM, the basement membrane. Tissue culture procedures which utilize reconstituted basement membrane matrices have been used to demonstrate that changes in matrix deposition, matrix degradation, cellular attachment to the matrix and migration through the matrix play a role in carcinoma cell invasion (Wyke, J.A. (2000) Eur. J. Cancer, 36:1589-1594).

does not define "cellular invasion" as invasion by a cell of other parts of a body. Cancer occurs when cells in a part of the body begin to grow out of control. Normal cells divide and grow in an orderly fashion, but cancer cells do not. They continue to grow and crowd out normal cells. Thus, applicant's definition is incorrect. Is the cell the invader or the cell being invaded?

Cellular invasion is very broad and it can include two definitions:

a. Cells being invaded by something else e.g. viruses, prions, etc., or

b. Cells are invading parts of the body (fungi, bacteria).

Applicants indicate choice b as the definition for cellular invasion and limited to cancer cells doing the invading, but there is no support for their choice (see above). The phrase "cellular invasion" covers both choices a and b and invasions by things other than cancer cells. Since cellular invasion can be defined according to choice a or b and the fact that applicant's choice of only cancer cell invasion has no support, the rejection is proper. The term clearly means more than applicant's stated intent.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571) 272-0674, if there is no reply within 24 hours, James Wilson (Acting SPE) can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kahsay Habte, Ph. D.
Examiner
Art Unit 1624

Mark L. Berch
Primary Examiner
Art Unit 1624

KH
September 29, 2004